

## CLAIMS:

1. A method of modifying cells of ocular tissue to produce an immunoglobulin or immunoglobulin fragment of interest, which comprises exposing ocular tissue to an effective concentration for transfection of an expression vector comprising a nucleotide sequence encoding for the immunoglobulin or immunoglobulin fragment, for a period sufficient to allow transfection, such that cells of said ocular tissue produce the immunoglobulin or immunoglobulin fragment.
2. The method according to claim 1 wherein the ocular tissue is selected from one or more of pupil, iris, vitreous, macula, retina, sclera, lens, choroid, limbal, conjunctiva and corneal tissue.
3. The method according to claim 1 wherein the ocular tissue is corneal tissue.
4. The method according to any one of claims 1 to 3 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of an MHC molecule, a co-stimulatory molecule, an adhesion molecule, a receptor-associated molecule, a cytokine receptor, interferon  $\gamma$  receptor, a viral surface antigen and a surface antigen of *Acanthamoeba*.
5. The method according to any one of claims 1 to 3 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of CD80, CD86, CD152, CD11b/e, CD18, CD54, CD62L, CD3, CD4, CD8, CD28, CD40, CD40L, ICOS, PD-1, BTLA, CTLA4, IL-2R, CD25, gD2 and gB2 antigen of herpes simplex virus and a surface antigen of the herpes virus causing herpetic keratitis.
6. The method according to any one of claims 1 to 5 wherein said ocular tissue is from a mammalian animal.

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7. The method according to any claim 6 wherein the mammalian animal is a human.
8. The method according to any one of claims 1 to 7 wherein the expression vector is a viral, bacterial or plasmid expression vector.
- 5 9. The method according to any one of claims 1 to 7 wherein the expression vector is an adeno-associated viral vector, an adenoviral, lentiviral or herpes simplex viral expression vector.
- 10 10. The method according to any one of claims 1 to 7 wherein the expression vector is a non-live expression vector.
11. The method according to any one of claims 1 to 7 wherein the expression vector is a liposomal expression vector.
- 15 12. The method according to any one of claims 1 to 11 wherein the effective concentration for transfection of the expression vector is between about  $1 \times 10^5$  to about  $1 \times 10^{10}$  pfu per gram of tissue.
- 20 13. The method according to any one of claims 1 to 12 wherein the exposing of said ocular tissue to an effective concentration for transfection of the expression vector is conducted *ex vivo*.
- 25 14. The method according to any one of claims 1 to 12 wherein the exposing of said ocular tissue to an effective concentration for transfection of the expression vector is conducted *in vivo*.
- 30 15. The method according to any one of claims 1 to 14 wherein the expression vector or another expression vector transfected into the ocular tissue comprises a nucleotide sequence encoding for an active agent, such that cells of said ocular tissue produce the active agent.

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16. The method according to claim 15 wherein the active agent is a peptide hormone, a cytokine or an analogue thereof.
- 5 17. The method according to claim 16 wherein the cytokine is selected from one or more of IL-10, IL-4, the P-40 component of IL-12, Bc12, interferon Gamma, interferon Alpha and TGF Beta.
- 10 18. The method according to any one of claims 1 to 17 wherein at least 10% of the cells of said ocular tissue are modified.
19. The method according to any one of claims 1 to 17 wherein at least 20% of the cells of said ocular tissue are modified.
- 15 20. The method according to any one of claims 1 to 17 wherein at least 50% of the cells of said ocular tissue are modified.
21. The method according to any one of claims 1 to 17 wherein at least 70% of the cells of said ocular tissue are modified.
- 20 22. The method according to any one of claims 1 to 21 wherein the modified cells are corneal endothelial cells.
23. The method according to any one of claims 1 to 22 wherein the nucleotide sequence is cDNA.
- 25 24. The method according to any one of claims 1 to 23 wherein the modified tissue is harvested from a donor and transplanted to an eye of a recipient animal.
- 30 25. A harvested ocular tissue comprising cells modified to produce an immunoglobulin or immunoglobulin fragment of interest.

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26. A harvested ocular tissue comprising cells modified by the method according to any one of claims 1 to 23.

5 27. A method of improving ocular graft healing and/or prolonging graft survival comprising exposing ocular tissue to an effective concentration for transfection of an expression vector comprising a nucleotide sequence encoding for an immunoglobulin or immunoglobulin fragment specific for an agent or agents associated with ocular graft healing and/or rejection, for a period sufficient to allow  
10 transfection such that cells of said ocular tissue will express the immunoglobulin or immunoglobulin fragment, harvesting said tissue from a donor and transplanting the ocular tissue to an eye of a recipient.

15 28. The method according to claim 27 wherein the ocular tissue is selected from one or more of pupil, iris, vitreous, macula, retina, sclera, lens, choroid, limbal, conjunctiva and corneal tissue.

29. The method according to claim 27 wherein the ocular tissue is corneal tissue.

20 30. The method according to any one of claims 27 to 29 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of an MHC molecule, a co-stimulatory molecule, an adhesion molecule, a receptor-associated molecule, a cytokine receptor, interferon  $\gamma$  receptor, a viral surface antigen and a surface antigen of *Acanthamoeba*.

25 31. The method according to any one of claims 27 to 29 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of CD80, CD86, CD152, CD11b/e, CD18, CD54, CD62L, CD3, CD4, CD8, CD28, CD40, CD40L, ICOS, PD-1, BTLA, CTLA4, IL-2R, CD25, gD2 and gB2 antigen of herpes simplex virus and a surface antigen of the herpes virus causing herpetic  
30 keratitis.

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32. The method according to any one of claims 27 to 31 wherein the ocular tissue is harvested from a mammalian animal.

5 33. The method according to claim 32 wherein the mammalian animal is a human.

34. The method according to any one of claims 27 to 33 wherein the expression vector is a viral, bacterial or plasmid expression vector.

10 35. The method according to any one of claims 27 to 33 wherein the expression vector is an adeno-associated viral vector, an adenoviral, lentiviral or herpes simplex viral expression vector.

15 36. The method according to any one of claims 27 to 33 wherein the expression vector is a non-live expression vector.

37. The method according to any one of claims 27 to 33 wherein the expression vector is a liposomal expression vector.

20 38. The method according to any one of claims 27 to 37 wherein the effective concentration for transfection of the expression vector is between about  $1 \times 10^5$  to about  $1 \times 10^{10}$  pfu per gram of tissue.

25 39. The method according to any one of claims 27 to 38 wherein the exposing of harvested ocular tissue to an effective concentration for transfection of the expression vector is conducted *ex vivo*.

30 40. The method according to any one of claims 27 to 38 wherein the exposing of said ocular tissue to an effective concentration for transfection of the expression vector is conducted *in vivo*.

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41. The method according to any one of claims 27 to 40 wherein the expression vector or another expression vector transfected into the ocular tissue comprises a nucleotide sequence encoding for an active agent, such that cells of said ocular tissue produce the active agent.

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42. The method according to claim 41 wherein the active agent is a peptide hormone, a cytokine or an analogue thereof.

43. The method according to claim 42 wherein the cytokine is selected from one or more of IL-10, IL-4, the P-40 component of IL-12, Bc12, interferon Gamma, interferon Alpha and TGF Beta.

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44. The method according to any one of claims 27 to 43 wherein at least 10% of the cells of said ocular tissue are modified.

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45. The method according to any one of claims 27 to 44 wherein at least 20% of the cells of said ocular tissue are modified.

46. The method according to any one of claims 27 to 44 wherein at least 50% of the cells of said ocular tissue are modified.

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47. The method according to any one of claims 27 to 44 wherein at least 70% of the cells of said ocular tissue are modified.

48. The method according to any one of claims 27 to 47 wherein the modified cells are corneal endothelial cells.

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49. The method according to any one of claims 27 to 28 wherein the nucleotide sequence is cDNA.

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50. The method according to any one of claims 27 to 49 wherein the modified tissue is transplanted to the eye of a recipient animal of same species as said donor.

5 51. A method of treatment and/or prophylaxis of an ocular disorder which comprises introducing into the eye of a mammalian patient an effective concentration for transfection into an ocular tissue of an expression vector comprising a nucleotide sequence encoding for an immunoglobulin or immunoglobulin fragment specific for an agent associated with the disorder, for a period sufficient to allow transfection such that cells of said ocular tissue will produce the immunoglobulin or immunoglobulin fragment.

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52. The method according to claim 51 wherein the ocular tissue is selected from one or more of pupil, iris, vitreous, macula, retina, sclera, lens, choroid, limbal, conjunctiva and corneal tissue.

15 53. The method according to claim 51 wherein the ocular tissue is corneal tissue.

54. The method according to any one of claims 51 to 53 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of an MHC molecule, a co-stimulatory molecule, an adhesion molecule, a receptor-associated molecule, a cytokine receptor, interferon  $\gamma$  receptor, a viral surface antigen and a surface antigen of Acanthamoeba.

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55. The method according to any one of claims 51 to 53 wherein the immunoglobulin or immunoglobulin fragment of interest has specificity for one or more of CD80, CD86, CD152, CD11b/e, CD18, CD54, CD62L, CD3, CD4, CD8, CD28, CD40, CD40L, ICOS, PD-1, BTLA, CTLA4, IL-2R, CD25, gD2 and gB2 antigen of herpes simplex virus and a surface antigen of the herpes virus causing herpetic keratitis.

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56. The method according to any one of claims 51 to 55 wherein the mammalian patient is a human.
57. The method according to any one of claims 51 to 56 wherein the expression vector  
5 is a viral, bacterial or plasmid expression vector.
58. The method according to any one of claims 51 to 56 wherein the expression vector is an adeno-associated viral vector, an adenoviral, lentiviral or herpes simplex viral expression vector.  
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59. The method according to any one of claims 51 to 56 wherein the expression vector is a non-live expression vector.
60. The method according to any one of claims 51 to 56 wherein the expression vector  
15 is a liposomal expression vector.
61. The method according to any one of claims 51 to 60 wherein the effective concentration for transfection of the expression vector is between about  $1 \times 10^5$  to about  $1 \times 10^{10}$  pfu per gram of tissue.  
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62. The method according to any one of claims 51 to 61 wherein the expression vector or another expression vector transfected into the ocular tissue comprises a nucleotide sequence encoding for an active agent, such that cells of said ocular ~~tissue produce the active agent~~  
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63. The method according to claim 62 wherein the active agent is a peptide hormone, a cytokine or an analogue thereof.
64. The method according to claim 63 wherein the cytokine is selected from one or  
30 more of IL-10, IL-4, the P-40 component of IL-12, Bcl2, interferon Gamma, interferon Alpha and TGF Beta.



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65. The method according to any one of claims 51 to 64 wherein at least 10% of the cells of said ocular tissue produce the immunoglobulin or immunoglobulin fragment.
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66. The method according to any one of claims 51 to 64 wherein at least 20% of the cells of said ocular tissue produce the immunoglobulin or immunoglobulin fragment.
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67. The method according to any one of claims 51 to 64 wherein at least 50% of the cells of said ocular tissue produce the immunoglobulin or immunoglobulin fragment.
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68. The method according to any one of claims 51 to 64 wherein at least 70% of the cells of said ocular tissue produce the immunoglobulin or immunoglobulin fragment.
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69. The method according to any one of claims 51 to 68 wherein said cells are corneal endothelial cells.
70. The method according to any one of claims 51 to 69 wherein the nucleotide sequence is cDNA.
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71. The method according to any one of claims 51 to 70 wherein introducing the expression vector into the eye is by topical administration of a cream, paste or tincture or of drops, comprising one or more pharmaceutically acceptable carriers and/or excipients.

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72. The method according to any one of claims 51 to 70 wherein introducing the expression vector into the eye is by direct injection into said ocular tissue of an injectable formulation comprising one or more pharmaceutically acceptable carriers and/or excipients.